

WEST Search History

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DATE: Tuesday, February 07, 2006

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
<i>DB=USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L2	Pas domain same human	25
<input type="checkbox"/>	L1	Pas domain same human same inhibitor	2

END OF SEARCH HISTORY

FILE 'EMBASE' ENTERED AT 08:56:42 ON 07 FEB 2006
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=> s pas domain
L1 297 FILE MEDLINE
L2 403 FILE CAPLUS
L3 280 FILE EMBASE

TOTAL FOR ALL FILES
L4 980 PAS DOMAIN

=> s 14 and human
TOTAL FOR ALL FILES
L8 291 L4 AND HUMAN

=> s 18 and kinase
TOTAL FOR ALL FILES
L12 55 L8 AND KINASE

=> s l12 not 2002-2006/py
TOTAL FOR ALL FILES
L16 20 L12 NOT 2002-2006/PY

=> dup rem l16
PROCESSING COMPLETED FOR L16
L17 9 DUP REM L16 (11 DUPLICATES REMOVED)

=> d ibib abs 1-9

L17 ANSWER 1 OF 9 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001433919 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11459942
TITLE: PAS kinase: an evolutionarily conserved
PAS domain-regulated serine/threonine
kinase.
AUTHOR: Rutter J; Michnoff C H; Harper S M; Gardner K H; McKnight S
L
CORPORATE SOURCE: Department of Biochemistry, University of Texas
Southwestern Medical Center, 5323 Harry Hines Boulevard,
Dallas, TX 75390-9152, USA.
CONTRACT NUMBER: DK52031 (NIDDK)
T32-GM08-291-12 (NIGMS)
SOURCE: Proceedings of the National Academy of Sciences of the
United States of America, (2001 Jul 31) 98 (16) 8991-6.
Electronic Publication: 2001-07-17.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-
AF387103
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010903
Last Updated on STN: 20030105
Entered Medline: 20010830

AB PAS domains regulate the function of many intracellular signaling pathways in response to both extrinsic and intrinsic stimuli. PAS domain-regulated histidine kinases are common in prokaryotes and control a wide range of fundamental physiological processes. Similarly regulated kinases are rare in eukaryotes and are to date completely absent in mammals. PAS kinase (PASK) is an evolutionarily conserved gene product present in yeast, flies, and mammals. The amino acid sequence of PASK specifies two PAS domains followed by a canonical serine/threonine kinase domain, indicating that it might represent the first mammalian PAS-regulated protein kinase. We present evidence that the activity of PASK is regulated by two mechanisms. Autophosphorylation at two threonine residues located within the activation loop significantly increases catalytic activity. We further demonstrate that the N-terminal PAS domain is a cis regulator of PASK catalytic activity. When the PAS domain-containing region is removed, enzyme activity is significantly increased, and supplementation of the purified PAS-A domain in trans selectively inhibits PASK catalytic activity. These studies define a eukaryotic signaling pathway suitable for studies of PAS domains in a purified *in vitro* setting.

L17 ANSWER 2 OF 9 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001389013 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11443095
TITLE: Competence repression under oxygen limitation through the two-component MicAB signal-transducing system in *Streptococcus pneumoniae* and involvement of the PAS domain of MicB.
AUTHOR: Echenique J R; Trombe M C
CORPORATE SOURCE: Laboratoire de Genetique et Physiologie Bacterienne, E.A. 3036, Centre Hospitalo Universitaire de Rangueil, Universite Paul Sabatier, 31403 Toulouse Cedex, France.
SOURCE: Journal of bacteriology, (2001 Aug) 183 (15) 4599-608.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816
AB In *Streptococcus pneumoniae*, a fermentative aerotolerant and catalase-deficient human pathogen, oxidases with molecular oxygen as substrate are important for virulence and for competence. The signal-transducing two-component systems CiaRH and ComDE mediate the response to oxygen, culminating in competence. In this work we show that the two-component MicAB system, whose MicB kinase carries a PAS domain, is also involved in competence repression under oxygen limitation. Autophosphorylation of recombinant MicB and phosphotransfer to recombinant MicA have been demonstrated. Mutational analysis and in vitro assays showed that the C-terminal part of the protein and residue L100 in the N-terminal cap of its PAS domain are both crucial for autokinase activity in vitro. Although no insertion mutation in micA was obtained, expression of the mutated allele micA59DA did not change bacterial growth and overcame competence repression under microaerobiosis. This was related to a strong instability of MicA59DA-PO(4) in vitro. Thus, mutations which either reduced the stability of MicA-PO(4) or abolished kinase activity in MicB were related to competence derepression under microaerobiosis, suggesting that MicA-PO(4) is involved in competence repression when oxygen becomes limiting. The micAB genes are flanked by mutY and orfC. MutY is an adenine glycosylase involved in the repair of oxidized pyrimidines. OrfC shows the features of a metal binding protein. We did not obtain insertion mutation in orfC, suggesting its requirement for growth. It is proposed that MicAB, with its PAS motif, may belong to a set of functions important in the protection of the cell against oxidative stress, including the control of competence.

L17 ANSWER 3 OF 9 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001694176 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11740943
TITLE: Regulation of *Drosophila* tracheal system development by protein kinase B.
COMMENT: Comment in: Dev Cell. 2001 Dec;1(6):726-8. PubMed ID: 11740932
AUTHOR: Jin J; Anthopoulos N; Wetsch B; Binari R C; Isaac D D; Andrew D J; Woodgett J R; Manoukian A S
CORPORATE SOURCE: Division of Cellular and Molecular Biology, Ontario Cancer Institute, University Health Network, Princess Margaret Hospital, Toronto, Ontario, M5G 2M9, Canada.
CONTRACT NUMBER: R01 DE12873 (NIDCR)
SOURCE: Developmental cell, (2001 Dec) 1 (6) 817-27.
Journal code: 101120028. ISSN: 1534-5807.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011217
Last Updated on STN: 20020125
Entered Medline: 20020114
AB Protein kinase B (PKB, also termed Akt) is a phosphatidylinositol 3' kinase (PI3'K)-dependent enzyme implicated in survival signaling and human tumorigenesis. To identify potential targets of this protein kinase, we employed a genetic screen in *Drosophila*. Among several genes that genetically interacted with PKB was trachealess (trh), which

encodes a bHLH- PAS domain transcription factor required for development of the trachea and other tubular organs. Trh activates expression of the fibroblast growth factor receptor Breathless, which, in turn, is required for directed migration of all tracheal branches. Using a combination of biochemical and transgenic approaches, we show that direct phosphorylation of Trh by PKB at serine 665 is essential for nuclear localization and functional activation of this regulator of branching morphogenesis.

L17 ANSWER 4 OF 9 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001639583 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11688972
TITLE: Mammalian PASKIN, a PAS-serine/threonine kinase
related to bacterial oxygen sensors.
AUTHOR: Hofer T; Spielmann P; Stengel P; Stier B; Katschinski D M;
Desbaillets I; Gassmann M; Wenger R H
CORPORATE SOURCE: Institute of Physiology, University of Zurich, Zurich,
CH-8057, Switzerland.
SOURCE: Biochemical and biophysical research communications, (2001
Nov 9) 288 (4) 757-64.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ318757
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020420
Entered Medline: 20011218
AB The PAS domain is a versatile protein fold found in many archaeal, bacterial, and plant proteins capable of sensing environmental changes in light intensity, oxygen concentration, and redox potentials. The oxygen sensor FixL from Rhizobium species contains a heme-bearing PAS domain and a histidine kinase domain that couples sensing to signaling. We identified a novel mammalian PAS protein (PASKIN) containing a domain architecture resembling FixL. PASKIN is encoded by an evolutionarily conserved single-copy gene which is ubiquitously expressed. The human PASKIN and mouse Paskin genes show a conserved intron-exon structure and share their promoter regions with another ubiquitously expressed gene that encodes a regulator of protein phosphatase-1. The 144-kDa PASKIN protein contains a PAS region homologous to the FixL PAS domain and a serine/threonine kinase domain which might be involved in signaling. Thus, PASKIN is likely to function as a mammalian PAS sensor protein.
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L17 ANSWER 5 OF 9 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights
reserved on STN
ACCESSION NUMBER: 2001070157 EMBASE Full-text
TITLE: The molecular basis of O(2)-sensing and hypoxia tolerance
in pheochromocytoma cells.
AUTHOR: Conrad P.W.; Conforti L.; Kobayashi S.; Beitner-Johnson D.;
Rust R.T.; Yuan Y.; Kim H.-W.; Kim R.H.; Seta K.; Millhorn
D.E.
CORPORATE SOURCE: D.E. Millhorn, Dept. of Molec./Cellular Physiology,
University of Cincinnati, College of Medicine, P.O. Box
67-0576, Cincinnati, OH 45267-0576, United States.
david.millhorn@uc.edu
SOURCE: Comparative Biochemistry and Physiology - B Biochemistry
and Molecular Biology, (2001) Vol. 128, No. 2, pp. 187-204.
.
Refs: 62
ISSN: 1096-4959 CODEN: CBPBB8
PUBLISHER IDENT.: S 1096-4959(00)00326-2
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 002 Physiology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322

AB Hypoxia is a common environmental stimulus. However, very little is known about the mechanisms by which cells sense and respond to changes in oxygen. Our laboratory has utilized the PC12 cell line in order to study the biophysical and molecular response to hypoxia. The current review summarizes our results. We demonstrate that the O(2)-sensitive K(+) channel, Kv1.2, is present in PC12 cells and plays a critical role in the hypoxia-induced depolarization of PC12 cells. Previous studies have shown that PC12 cells secrete a variety of autocrine/paracrine factors, including dopamine, norepinephrine, and adenosine during hypoxia. We investigated the mechanisms by which adenosine modulates cell function and the effect of chronic hypoxia on this modulation. Finally, we present results identifying the mitogen- and stress-activated protein kinases (MAPKs and SAPKs) as hypoxia-regulated protein kinases. Specifically, we show that p38 and an isoform, p38 γ , are activated by hypoxia. In addition, our results demonstrate that the p42/p44 MAPK protein kinases are activated by hypoxia. We further show that p42/p44 MAPK is critical for the hypoxia-induced transactivation of endothelial PAS-domain protein 1 (EPAS1), a hypoxia-inducible transcription factor. Together, these results provide greater insight into the mechanisms by which cells sense and adapt to hypoxia. .COPYRGT. 2001 Elsevier Science Inc.

L17 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:361126 CAPLUS Full-text

DOCUMENT NUMBER: 135:150447

TITLE: Differential expression of multiple genes during articular chondrocyte redifferentiation

AUTHOR(S): Haudenschild, Dominik R.; Mcpherson, John M.; Tubo, Ross; Binette, Francois

CORPORATE SOURCE: Genzyme Tissue Repair, Framingham, MA, USA

SOURCE: Anatomical Record (2001), 263(1), 91-98

CODEN: ANREAK; ISSN: 0003-276X

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Articular chondrocytes undergo a rapid change in phenotype and gene expression, termed dedifferentiation, when isolated from cartilage tissue and cultured on tissue culture plastic. On the other hand, "redifferentiation" of articular chondrocytes in suspension culture is characterized by decreased cellular proliferation and the reinitiation of synthesis of hyaline articular cartilage extracellular matrix mols. The mol. triggers for these events have yet to be defined. Subtracted cDNA libraries representing genes involved in the early events of adult human articular chondrocyte redifferentiation were generated from human articular chondrocytes that were first cultured in monolayer, and subsequently transferred to suspension culture at 10⁶ cells/mL for redifferentiation. Differential regulation of genes involved in cellular organization, nuclear structure, cellular growth regulation, and extracellular matrix deposition and remodeling were observed within 48 h of this transfer. Many of these genes had not been previously identified in the chondrocyte differentiation pathway and a number of the isolated cDNAs did not have homologies to sequences in the public data banks. Genes involved in IL-6 signal transduction including acute phase response factor (APRF), Mn superoxide dismutase, and IL-6 itself were up-regulated in suspension culture. Membrane glycoprotein gp130, a component of the IL-6 receptor, was down-regulated. Other genes involved in cell polarity, cell adherence, apoptosis, and possibly TGF-beta signaling were differentially regulated. The differential regulation of the cytokine connective tissue growth factor (CTGF) during the early stages of articular chondrocyte redifferentiation, decreasing within 48 h of transfer to suspension culture, was particularly interesting given its reported role in the stimulation of cellular proliferation. CTGF was highly expressed in proliferative monolayer culture, and then greatly reduced by redifferentiation in standard high-d. suspension culture. When articular chondrocytes were seeded in suspension at low-d. (10⁴ cells/mL), however, high levels of CTGF were observed along with increased levels of mature articular cartilage extracellular matrix protein RNAs, such as type II collagen and aggrecan. Although the role of CTGF in articular cartilage biol. remains to be elucidated, the results described here demonstrate the potential utility of subtractive hybridization in understanding the process of articular chondrocyte redifferentiation.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 9 MEDLINE on STN

ACCESSION NUMBER: 2000045094 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10574786

TITLE: Fix L, a haemoglobin that acts as an oxygen sensor: signalling mechanism and structural basis of its homology with PAS domains.

AUTHOR: Perutz M F; Paoli M; Lesk A M

CORPORATE SOURCE: MRC Laboratory of Molecular Biology, Cambridge, CB2 2QH, UK.
SOURCE: Chemistry & biology, (1999 Nov) 6 (11) R291-7. Ref: 29
Journal code: 9500160. ISSN: 1074-5521.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000209
Last Updated on STN: 20000209
Entered Medline: 20000131
AB Fix L, which contains a haemoglobin domain homologous to the PAS family and a histidine kinase domain, forms, with Fix J, a two-component signalling complex that regulates expression of nitrogenase genes in Rhizobium. Spin transitions of its haem iron trigger stereochemical changes in and around the haem that, together with steric effects, control the activity of the kinase. Homology with the PAS family is based on a common core of about 20 structurally equivalent sites from which polar residues are excluded.

L17 ANSWER 8 OF 9 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 97179451 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9027737
TITLE: Structural and functional analysis of hypoxia-inducible factor 1.
AUTHOR: Semenza G L; Agani F; Booth G; Forsythe J; Iyer N; Jiang B H; Leung S; Roe R; Wiener C; Yu A
CORPORATE SOURCE: Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
SOURCE: Kidney international, (1997 Feb) 51 (2) 553-5. Ref: 27
Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970602
Last Updated on STN: 19970602
Entered Medline: 19970519
AB Hypoxia-inducible factor 1 (HIF-1) is a basic helix-loop-helix protein that activates transcription of hypoxia-inducible genes, including those encoding: erythropoietin, vascular endothelial growth factor, heme oxygenase-1, inducible nitric oxide synthase, and the glycolytic enzymes aldolase A, enolase 1, lactate dehydrogenase A, phosphofructokinase I, and phosphoglycerate kinase 1. Hypoxia response elements from these genes consist of a HIF-1 binding site (that contains the core sequence 5'-CGTG-3') as well as additional DNA sequences that are required for function, which in some elements include a second HIF-1 binding site. HIF-1 is a heterodimer. The HIF-1 alpha subunit is unique to HIF-1, whereas HIF-1 beta (ARNT) can dimerize with other bHLH-PAS proteins. Structural analysis of HIF-1 alpha revealed that dimerization with HIF-1 beta (ARNT) requires the HLH and PAS domains, DNA binding is mediated by the basic domain, and that HIF-1 alpha contains a carboxyl-terminal transactivation domain. Co-transfection of HIF-1 alpha and HIF-1 beta (ARNT) expression vectors and a reporter gene containing a wild-type hypoxia response element resulted in increased transcription in non-hypoxic cells and a superinduction of transcription in hypoxic cells, whereas HIF-1 expression vectors had no effect on the transcription of reporter genes containing a mutation in the HIF-1 binding site. HIF-1 alpha and HIF-1 beta (ARNT) protein levels were induced by hypoxia in all primary and transformed cell lines examined. In HeLa cells, the levels of HIF-1 alpha and HIF-1 beta protein and HIF-1 DNA-binding activity increased exponentially as cellular oxygen tension decreased, with maximum values at 0.5% oxygen and half-maximal values at 1.5 to 2% oxygen. HIF-1 alpha and HIF-1 beta (ARNT) mRNAs were detected in all human, mouse, and rat organs assayed and mRNA expression was modestly induced in rodents subjected to hypoxia. HIF-1 alpha protein levels were induced in vivo when animals were subjected to anemia or hypoxia. The HIF1A gene was mapped to human chromosome 14q21-q24 and mouse chromosome 12.

L17 ANSWER 9 OF 9 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 97152468 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 9000051
TITLE: Endothelial PAS domain protein 1
(EPAS1), a transcription factor selectively expressed in
endothelial cells.
AUTHOR: Tian H; McKnight S L; Russell D W
CORPORATE SOURCE: Department of Molecular Genetics, University of Texas
Southwestern Medical Center, Dallas 75235, USA.
CONTRACT NUMBER: CA52121 (NCI)
DK-47657 (NIDDK)
SOURCE: Genes & development, (1997 Jan 1) 11 (1) 72-82.
Journal code: 8711660. ISSN: 0890-9369.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U81983; GENBANK-U81984
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 19990129
Entered Medline: 19970213

AB Here we describe the cloning and characterization of a PAS domain transcription factor termed endothelial PAS-1 (EPAS1). This protein shares 48% sequence identity with hypoxia inducible factor (HIF-1alpha) and lesser similarity with other members of the basic helix-loop-helix/PAS domain family of transcription factors. Like HIF-1alpha, EPAS1 binds to and activates transcription from a DNA element originally isolated from the erythropoietin gene and containing the sequence 5'-GCCCTACGTGCTGTCTCA-3'. Activation by both HIF-1alpha and EPAS1 is stimulated by hypoxic conditions. EPAS1 forms a heterodimeric complex with the aryl hydrocarbon nuclear transporter prior to transcriptional activation of target genes. EPAS1 expression is limited to the endothelium of mouse embryos and, in agreement with its cell type-specific expression pattern, is capable of specifically activating the transcription of the endothelial tyrosine kinase gene Tie-2. These observations raise the possibility that EPAS1 may represent an important regulator of vascularization, perhaps involving the regulation of endothelial cell gene expression in response to hypoxia.

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=> s 18 and inhibitor
L18          7 FILE MEDLINE
L19          17 FILE CAPLUS
L20          4 FILE EMBASE
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TOTAL FOR ALL FILES
L21          28 L8 AND INHIBITOR
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=> s 121 not 2002-2006/py
TOTAL FOR ALL FILES
L25          4 L21 NOT 2002-2006/PY
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=> dup rem 125
PROCESSING COMPLETED FOR L25
L26          2 DUP REM L25 (2 DUPLICATES REMOVED)
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=> d ibib abs 1-2
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L26 ANSWER 1 OF 2      MEDLINE on STN
ACCESSION NUMBER: 2001222592      MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11312108
TITLE: The Ets family contains transcriptional activators and  
repressors involved in angiogenesis.
AUTHOR: Lelievre E; Lionneton F; Soncin F; Vandembunder B
CORPORATE SOURCE: Institut de Biologie de Lille, 1, rue du Professeur  
Calmette, BP 447, 59021, Lille Cedex, France.
SOURCE: international journal of biochemistry & cell biology, (2001  
Apr) 33 (4) 391-407. Ref: 67
Journal code: 9508482. ISSN: 1357-2725.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(FILE TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
```

ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010625
Last Updated on STN: 20010625
Entered Medline: 20010621

AB The Ets family contains a growing number of transcriptional activators and inhibitors, which activity is regulated by phosphorylation and protein-protein interactions. Among these factors, Ets1, Erg1 and Flil are expressed in endothelial cells during angiogenesis in normal and pathological development. The expression of these transcription factors is regulated by angiogenic factors in cultured endothelial cells, as well as by various stresses occurring during angiogenesis. Transfection experiments and transgenic mice analysis revealed that Ets family members are involved in the transcriptional regulation of endothelial specific genes such as those encoding Tie1 and -2, VEGFR1 and -2 and VE-Cadherin. In vitro studies plead for a role of Ets family members in endothelial cell adhesion, spreading and motility. Gene inactivation experiments show that Ets1 is dispensable for embryonic development. The phenotype of knocked-out embryos indicates that Tel is required for maintenance of the developing vascular network in the yolk sac. Altogether, we suggest that Ets family members act both positively and negatively during the different steps of the angiogenic process. The regulation of the initiation of gene transcription arises from the combined activity of different transcriptional regulators. Therefore very few transcription factors are specific for a physiological process, or a given cell type. The transcriptional network that regulates blood vessel formation involves transcription factors which are expressed in a variety of situations. The Lung Kruppel Like Factor (LKLF) which is required for blood vessel stabilisation during murine development is also expressed in the primitive vertebrae and in the lung of the adult (C.T. Kuo, M.L. Veselits, K.P. Barton, M.M. Lu, C. Clendenin, J.M. Leiden, The LKLF transcription factor is required for normal tunica media formation and blood vessel stabilisation during murine embryogenesis, *Genes Dev.* 11 (22) (1997) 2996-3006). Scl/Tall which is essential for angiogenic remodelling of the yolk sac capillary network (J.E. Visvader, Y. Fujiwara, S.H. Orkin, Unsuspected role for the T-cell leukemia protein SCL/tal-1 in vascular development, *Genes Dev.* 12 (4) (1998) 473-479), is involved in blood cell development and is also expressed in the developing brain. The EPAS transcription factor which was thought to be endothelial cell specific in the mouse embryo (H. Tian, S.L. McKnight, D.W. Russell, Endothelial PAS domain protein 1 (EPAS1), a transcription factor selectively expressed in endothelial cells, *Genes Dev.* 11 (1) (1997) 72-82) is also expressed in the liver, kidney and cells of the sympathetic nervous system of the chick embryo (J. Favier, H. Kempf, P. Corvol, J.M. Gasc, Cloning and expression pattern of EPAS1 in the chicken embryo. Colocalization with tyrosine hydroxylase, *FEBS Lett.* 462 (1-2) (1999) 19-24). Ets1, which expression was originally detected in lymphoid cells of adult tissues, has been the first transcription factor to be identified in endothelial cells during angiogenesis in the embryo (B. Vandenbunder, L. Pardanaud, T. Jaffredo, M.A. Mirabel, D. Stehelin, Complementary patterns of expression of c-ets1, c-myb and c-myc in the blood-forming system of the chick embryo, *Development* 107 (1989) 265-274 [5]) and in tumours (N. Wernert, M.B. Raes, P. Lassalle, M.P. Dehouck, B. Gosselin, B. Vandenbunder, D. Stehelin, The c-ets 1 proto-oncogene is a transcription factor expressed in endothelial cells during tumor vascularisation and other forms of angiogenesis in man, *Am. J. Path.* 140 (1992) 119-127 [6]). Since then, the Ets family has extended and this review will emphasise the relationships between these factors and angiogenesis.

L26 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001082703 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11018023
TITLE: CLIF, a novel cycle-like factor, regulates the circadian oscillation of plasminogen activator inhibitor-1 gene expression.
AUTHOR: Maemura K; de la Monte S M; Chin M T; Layne M D; Hsieh C M; Yet S F; Perrella M A; Lee M E
CORPORATE SOURCE: Cardiovascular and the Pulmonary and Critical Care Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA..
kmae-tky@umin.ac.jp
CONTRACT NUMBER: HL 03745 (NHLBI)
HL 10113 (NHLBI)
HL 60788 (NHLBI)
+
SOURCE: Journal of biological chemistry, (2000 Nov 24) 275 (47)
36847-51.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF256215
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010108

AB The onset of myocardial infarction occurs frequently in the early morning, and it may partly result from circadian variation of fibrinolytic activity. Plasminogen activator inhibitor-1 activity shows a circadian oscillation and may account for the morning onset of myocardial infarction. However, the molecular mechanisms regulating this circadian oscillation remain unknown. Recent evidence indicates that basic helix-loop-helix (bHLH)/PAS domain transcription factors play a crucial role in controlling the biological clock that controls circadian rhythm. We isolated a novel bHLH/PAS protein, cycle-like factor (CLIF) from human umbilical vein endothelial cells. CLIF shares high homology with Drosophila CYCLE, one of the essential transcriptional regulators of circadian rhythm. CLIF is expressed in endothelial cells and neurons in the brain, including the suprachiasmatic nucleus, the center of the circadian clock. In endothelial cells, CLIF forms a heterodimer with CLOCK and up-regulates the PAI-1 gene through E-box sites. Furthermore, Period2 and Cryptochromel, whose expression show a circadian oscillation in peripheral tissues, inhibit the PAI-1 promoter activation by the CLOCK:CLIF heterodimer. These results suggest that CLIF regulates the circadian oscillation of PAI-1 gene expression in endothelial cells. In addition, the results potentially provide a molecular basis for the morning onset of myocardial infarction.

=> log y